Decreased formation of phosphatidylinositol-phosphate (PIP) but not phosphatidylinositol-bisphosphate (PIP2) in Alzheimer's disease brain versus control brain

A

IBOTENATE INDUCED STIMULATION OF MONO-AND DIACYLGLYCEROL LIPASES IN RAT BRAIN. A.A. Farooqui*, L. Wallace* and L.A. Horrocks. Dept. of Med. Biochem. and Div. Pharmacol., The Ohio State University, Columbus, Ohio 43210, U.S.A.

Direct administration of ibotenate into the nucleus basalis magnocellularis of rat brain causes extensive neurodegeneration by destroying cholinergic cell bodies and has been used to develop a potential animal model for Alzheimer's disease (AD). A marked increase of mono- and diacylglycerol lipase activities is found in nucleus basalis and hippocampus regions of autopsy brain from AD patients (Ann. Neurol. (1985) 23:306-308). We have injected ibotenate in the nucleus basalis magnocellularis region of rat brain to study whether an elevation of lipases was associated with the degeneration of cholinergic neurons in this potential animal model of AD. Two plasma membrane fractions were prepared from different regions of ibotenate injected (right hemisphere) and control (left hemisphere) rat brain. One plasma membrane fraction was from synaptosomes (SPM) and the other from glial cell and neuronal cell bodies (PM). Activities of mono and diacylglycerol lipases in the above plasma membrane fractions were markedly increased (3-5 fold) in hippocampus, mid brain and frontal cortex regions of ibotenate injected rat brain after 10 days. The activity of choline acetyltransferase was decreased in frontal cortex but unchanged in hippocampus and midbrain. Our results suggest that the increase in lipase activity is much more widespread than is the decrease in cholinergic function. Supported by The Ohio Department of Aging, State of Ohio.

B

AGGREGATION PROPERTIES OF GANGLIOSIDES AND THEIR RELEVANCE TO COMPOSITION OF NEURONAL MEMBRANES L.Cantù*,M.Corti*,S.Sonnino*,andG.Tettamanti,Dpt. of Chem.and Biochem. University of Milan,via Saldini 50, 20133 Milan, Italy

Gangliosides are amphiphilic molecules which spontaneously aggregate in solution. A careful study of this process for different gangliosides and mixtures of them can be helpful in understanding their role in natural membranes. It is found ,for istance, that the geometrical dimensions of the hydrophilic and hydrophobic parts of the molecule are important in determining size and shape of the aggregate. Larger oligosaccharide chains allow larger curvatures and viceversa.This has been experimentally verified with the ganglioside series GT1b,GD1a,GM1,GM2. They form micelles of inceasing size and non-sphericity. Mixing of GT1b and GM2 gives rise to flat micelles with GT1b spontaneously segregated in the region of larger curvature, namely at the edges. Similar effects may occur in natural systems in connection with the non-uniform curvature of the membrane microenviroment. Also interesting is that GM3 forms small vesicles spontaneously with a bending elasticity much smaller than the typical one of phospholipids.This may be of relevance in the case of clustering of GM3 on the mambrane.Besides, it is important to notice that hydrophobic chains in GM3 vesicles are fully interdigitated, which means that the membrane thickness is very small.

C

DECREASED FORMATION OF PHOSPHATIDYLINOSITOLPHOSPHATE (PIP) BUT NOT PHOSPHATIDYLINOSITOLBISPHOSPHATE (PIP_2) IN ALZHEIMER'S DISEASE BRAIN VERSUS CONTROL BRAIN. J. Jolles*, J.G.M. Bothmer* and M. Markerink*. University of Limburg, P.O. Box 616, 6200 MD Maastricht, the Netherlands.

There is an increasing number of neurochemical studies into the pathogenesis of Alzheimer's Disease (AD). Up till now, however, there is only a very limited number of studies into active enzymic processes in these conditions. The present study investigates phospholipidphosphorylation processes. The premise is that a decrease in brain membrane function might underlie the decrease in brain function with age and especially AD, and that memory function is dependent upon the rapid interconversion of inositolphospholipids. The assay system used, consists of incubation of a cytosolic fraction (containing the relevant enzymes PI-kinase and PIP-kinase) under hypotonic conditions for short time periods with gamma-labelled ^{32}P-ATP. A membrane-free S1 was used (100,000 g sup) with exogenous PI and PIP as lipid substrate. In the first experiment, 5 AD patients aged 55 - 78, were compared with carefully matched control subjects. It appeared that there was a dramatic decrease in ^{32}P-PIP formation in AD patients as compared to controls (40 - 55% reduction in 4 neocortical areas, i.e., prefrontal cortex, precentral cortex, temporal cortex and occipital cortex). In contrast, the formation of ^{32}P-PIP_2 was identical in AD patients and controls in the four cortical areas tested. In a second experiment, it was investigated whether the factor "age" has any effect in addition to the factor "disease". Temporal cortical tissue obtained from 16 patients aged 54 - 90 was compared with respect to PIP and PIP_2 formation. There was a negative correlation between age and the formation of both phosphoinositides, indicating that the formation of both lipids decreases with age. (circa 20% reduction between 55 and 90 years). All brain material had been obtained with a short port mortem duration within 6 hours after death (range 3.5 to 6 hours); the factor post mortem interval appeared not to have any influence on the enzyme activities measured. The results could be of substantial importance for studies into (patho)physiological brain aging and AD because of the selective effects on lipidphosphorylation and the relevance of the polyphosphoinositides for brain membrane function.

D

LABELING OF RETINA GANGLION CELL PHOSPHOLIPIDS IN CHICKENS EXPOSED TO LIGHT STIMULATION. Mario E. Guido*& Beatriz L. Caputto*. Facultad de Ciencias Quimicas, Universidad Nacional de Cordoba, C.C. 61, Cordoba, ARGENTINA.

We have found that light stimulation increases in vivo the labeling of phospholipids in the chick retina ganglion cells compared to dark maintained animals (light > dark 51% ; $p<0.001$). This in its turn originates an increase in the amount of label that arrives by axonal transport to the contralateral optic tectum in light (light > 30% ; $p<0.01$) No individual phospholipid accounts for the differences observed in the labeling of the total phospholipid pool. No systemic effector was found responsible of the differences observed in the labeling of these lipids between both illumination conditions. These differences are independent of the nerve endings because they are maintained even in chickens with one of their optic nerves ligated. The results are interpreted as an increase in the biosynthesis of phospholipids in the ganglion cell somas of animals in light respect to dark.

In order to elucidate the mechanisms that could be operating in the regulation of these phenomena, the incorporation in vitro of 32P into phospholipids of retina ganglion cell homogenates was determined. It was found a higher labeling of these lipids in the ganglion cells that were from light. The biosynthetic activity and the differences in labeling of phospholipids were observed in the microsomal fraction obtained after centrifugation of the homogenates at 200,000 x g during 45 min.